CHPA
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Producers of Quality Nonprescription Medicines and Dietary Supplements for Self-Care

CONSUMER HEALTHCARE PRODUCTS ASSOCIATION
Formerly Nonprescription Drug Manufacturers Association

October 20, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. 99N-1819: Topical Antifungal Drug Products for Over-the-Counter Human Use

Dear Sir or Madam:

The Consumer Healthcare Products Association (CHPA) submits these comments in response to the notice of proposed rulemaking [64 *Fed. Reg.* 39452-39454] published July 22, 1999, by the Food and Drug Administration (FDA) regarding a specific change in labels for over-the-counter (OTC) topical antifungal drug products. CHPA, founded in 1881, is the national trade organization representing manufacturers and distributors of OTC drug products and dietary supplements. CHPA members account, by sales, for over 90% of the OTC drugs marketed in the United States. CHPA has actively participated in all aspects of the agency's OTC Drug Review and represents the major manufacturers of OTC topical antifungal drug products. CHPA's comments are not meant to supersede any comments that might be submitted by CHPA member companies in response to the proposed rulemaking.

FDA's proposed rule would amend the Final Monograph (September 23, 1992) for topical antifungal products to require the addition of the word "most" in the allowed indications statement, between the introductory phrase and the name of the condition(s) for which the antifungal product is to be used.

Requested Action

CHPA urges FDA to decide against issuing a Final Rule requiring the addition of "most" in OTC topical antifungal indication statements, for the following reasons:

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- Scientific documentation is lacking to show that adding the qualifier "most" would meet an important consumer need.
- The use of qualified indication statements is unprecedented in the OTC Review.
- A qualified indications statement is potentially misleading, in that it implies inherent lack of efficacy of the active ingredient.
- The proposed amendment would create differences in labeling among products marketed under the monograph and those with an approved NDA, which could create consumer confusion.

Background

The proposed monograph amendment would require the inclusion of "most" in such label statements as:

"Treats most athelete's foot" [or ". . . most jock itch" or ". . . most ringworm"]

"For the effective treatment of most athelete's foot" [or ". . . most jock itch" or ". . . most ringworm"]

"Cures most athelete's foot" [or ". . . most jock itch" or ". . . most ringworm"]

"Proven clinically effective in the treatment of most athelete's foot" [or ". . . most jock itch" or ". . . most ringworm"]

"Clinically proven to prevent most athelete's foot . . ."

"For the prevention of most athelete's foot . . . "

[Emphasis added.]

In its preamble to the proposed amendment to the Final Monograph, FDA mentions that the Advisory Review Panel on OTC Antimicrobial (II) Drug Products ("the Panel") discussed conditions that could be mistaken for athlete's foot or jock itch, but said that the Panel did not address consequences of "misdiagnosis" of those conditions. The agency subsequently concluded that because some misdiagnosed conditions cannot be effectively treated with a

topical antifungal product, the word "most" should be added "to more accurately inform" consumers about "what they can expect from using these products." [64 *Fed. Reg.* 39452]

The agency failed to mention, however, that the Panel concluded such modifying words as "most" or "fast" should not be allowed in claims statements, because they can make claims "unclear or even imprecise." The Panel declared "Kills most athlete's foot fungi" an unacceptable label statement. [47 *Fed. Reg.* 12524]

Qualified Statements are Potentially Misleading.

CHPA agrees with the Panel's conclusion. Adding the word "most" would not advance the goal to "more accurately inform" consumers about these products. On the contrary, the addition of "most" in each case (shown in the examples on page 2) would imply that the drug product was of questionable effectiveness. This is inconsistent with the regulatory definition for effectiveness. "Effectiveness" is defined to mean "a reasonable expectation that, in a significant proportion of the target population, the pharmacological effect of the drug, when used under adequate directions for use and warnings against unsafe use, will provide clinically significant relief of the type claimed" 21 CFR §330.10(a)(4).

The standard for effectiveness does not require that every user of an OTC topical antifungal product gets complete relief (or prevention) for the condition for which he or she chose the product. The condition may not clear up because it is one that is not appropriately treated with a topical antifungal, but partial effectiveness or lack of effectiveness could be due to other reasons. For example, a consumer may not get relief for a treatable condition if the product is used incorrectly, i.e., not in accordance with the label directions. OTC product labels provide warnings about seeking the advice of a physician if the drug is not providing relief. The current Final Monograph for OTC topical antifungals requires a statement on the label directing the consumer to consult a doctor if the product is not effective within the recommended treatment period, for example, "If irritation occurs or if there is no improvement within 2 weeks, discontinue use and consult a doctor." (The new OTC label format, required under 21 CFR

§201.66, will highlight this statement through the special warning subheading, "Stop use and ask a doctor if . . . . ")

Qualified Indication Statements are Unprecedented in OTC Monographs.

No other OTC drug monograph requires a statement that qualifies the effect of a drug category [such as, for example, "relief of most headaches" for internal analgesics]. Why should topical antifungal products be required to have a statement implying they are somewhat ineffective when the OTC policy for labeling has consistently omitted qualifiers to effectiveness?

Scientific Data are Lacking.

FDA has not documented that the proposed amendment is important for safe and effective use of the products by consumers. In the preamble to the December 12, 1989, Tentative Final Monograph for OTC topical antifungal drug products, FDA stated ". . . OTC drug monographs directly address only those labeling items that are related in a significant way to the safe and effective use of covered products by lay persons." [54 *Fed. Reg.* 51154] The agency at that time listed "kills most athlete's foot fungi" among statements "describing the performance of the product" and not relating "in a significant way to the safe and effective use of antifungal drug products that are already labeled with the required information, and, therefore, are outside the scope of the monograph." [54 *Fed. Reg.* 51154]

Alteration of the required labeling information, including the indications statement, should be based on the same level of scientific documentation, clinical significance, and importance for the proper use by consumers as FDA uses for label warnings under its policy that "[w]arning statements for OTC drug products should be limited to those that are scientifically documented, clinically significant, and important for the safe and effective use of the products by consumers." [47 *Fed. Reg.* 54754 (1982); 53 *Fed. Reg.* 46213 (1988)] By its own standard, as stated in the antifungal Tentative Final Monograph cited in the preceding paragraph, FDA must show that the addition of "most" relates in a significant way to the safe and effective use of OTC topical

antifungal products. The agency did not provide such information in support of the proposed amendment.

In the absence of a substantial, well documented reason, it is inappropriate to require the addition of the word "most" to the label statement on OTC topical antifungal drug products. FDA currently has no data to show that adding the word "most" has any value in assisting consumers in better use of OTC topical antifungal drug products. The proposed revision is unlikely to change consumers' expectations for the products or to change the way products are selected to treat or prevent symptoms of athlete's foot, jock itch, or ringworm. There's no evidence to show that current antifungal indication statements without the word "most" are confusing. Adding such a qualifier would run counter to indication statements for all other OTC monograph categories, which do not have such qualifiers.

The Amendment Would Create Differences Between Monograph and NDA Labeling.

This rulemaking also presents an important matter of procedure, fairness, and avoidance of consumer confusion. Some OTC topical antifungal drug products are marketed under the Final Monograph and others are marketed under NDAs, sometimes under the same brandname. The proposed rule applies only to the monograph products and does not provide for managing the inconsistency that would be produced between monograph and NDA products with different labeling. FDA should coordinate label changes for OTC products within a therapeutic category and not require word-at-a-time, piecemeal label changes for monograph products. Monograph labels that are inconsistent with NDA labels for the same category of products could confuse consumers, who could mistakenly believe that antifungal products marketed under an NDA are more effective than the monograph products, which would be labeled to treat only "most" covered conditions.

Conclusions

In conclusion, CHPA recommends that FDA not require the additional word "most" in indication statements for OTC topical antifungal drug products. As discussed in these comments:

- Scientific documentation is lacking to show that such a qualifier would meet an important consumer need;
- The use of qualified indication statements is unprecedented in the OTC Review; and
- A qualified indications statement is potentially misleading, in that it implies inherent lack of efficacy of the active ingredient.

Further, the proposed amendment would create differences in labeling among products marketed under the monograph and those with an approved NDA, which could cause consumer confusion.

CHPA knows of no benefit to consumers in the use of the word "most" in the labeling of OTC topical antifungal drug products and asks FDA to decide against finalizing the amendment in regulation.

Sincerely,

Lorna C. Totman

Lorna C. Totman, Ph.D., DABT
Director of Scientific Affairs

Comments on most
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